Claims

1. An FrpB protein having one or more deletions of non-conserved amino acids compared to a corresponding wild-type FrpB protein.

2. An FrpB protein in which one or more of the amino acids of at least one of its loops has been deleted.

3. The protein according to claim 1 or 2 which is cross-protective.

4. The protein according to any preceding claim in which one or more of the amino acids of at least 2 loops have been deleted.

5. The protein according to any preceding claim in which one or more of the amino acids of loop 7 and/or 5 have been deleted.

6. The protein according to any preceding claim in which one or more the amino acids of any one or more of loops 1, 2, 3, 4, 6, 8, 9, 10, 11, 12 and 13 have been deleted.

7. The protein according to any preceding claim in which 11 to 33 amino acids have been deleted from loop 7.

8. The protein according to any preceding claim in which 23-33 amino acids have been deleted from loop 7.

9. The protein according to any preceding claim in which about 28 amino acids have been deleted from loop 7.

10. The protein according to any preceding claim in which 18-29 amino acids have been deleted from loop 5.

11. The protein according to any preceding claim in which 19-29 amino acids have been deleted from loop 5.

12. The protein according to any preceding claim in which 24 amino acids have been deleted from loop 5.

13. The protein according to any preceding claim in which, with reference to FrpB strain H44/76, the amino acid deletion is made in the range of amino acids 376-413, or a corresponding deletion made, from loop 7.

14. The protein according to any preceding claim in which, with reference to FrpB strain H44/76, the amino acid deletion is made in the range of amino acids 381-408, or a corresponding deletion made, from loop 7.

15. The protein according to any preceding claim in which, with reference to FrpB strain H44/76, an amino acid sequence comprising TTEEKNGQKVDKPMEQQMKDRADEDTVH has been deleted, or a corresponding deletion made, from loop 7.

16. The protein according to any preceding claim in which, with reference to FrpB strain H44/76, the amino acid deletion is made in the range of amino acids 247-280, or a corresponding deletion made, from loop 5.

17. The protein according to any preceding claim in which, with reference to FrpB strain H44/76, the amino acid deletion is made in the range of amino acids 252-275, or a corresponding deletion made, from loop 5.

18. The protein according to any preceding claim in which, with reference to FrpB strain H44/76, an amino acid sequence comprising QHRGIRTVREEFTVGDKSSRINID has been deleted, or a corresponding deletion made, from loop 5.

19. The protein of any preceding claim in which the deleted sequence is replaced by another amino acid sequence.

20. The protein of claim 19 in which the sequence is deleted by mutagenesis.

21. A polynucleotide encoding the protein of any preceding claim.

22. An expression vector comprising the polynucleotide of claim 21

23. A host cell comprising the expression vector of claim 22.

24. A method for producing the protein of any one of claims 1 to 20 comprising: culturing the host cell of claim, and recovering the expressed protein.

25. A method for refolding an FrpB protein comprising contacting the FrpB protein with an alkaline refolding buffer comprising 3-dimethyldodecylammoniopropanesulfonate (Zwittergent 3-12 or SB-12).

26. A method according to claim 25 wherein the protein is a protein according to any one of claims 1 to 20.

27. A method according to claim 25 or 26 wherein the refolding buffer comprises ethanolamine and SB-12.

28. A method according to claim 27 wherein the ethanolamine is about 20mM ethanolamine.

29. A method according to any one of claims 25 to 28 wherein the refolding buffer has pH11.

30. A method according to any one of claims 25 to 29 wherein the SB-12 is 0.2% SB-12.

31. A method according to any one of claims 25 to 29 wherein the SB-12 is 0.5% SB-12.

32. A method according to any one of claims 25 to 31 wherein the refolding buffer further comprises guanidium chloride, NaCl and/or urea.

33. A method according to claim 32 wherein the refolding buffer further comprises guanidium chloride.

34. A method according to claim 33 wherein the refolding buffer further comprises 0.4M guanidium chloride.

35. A method of any one of claims 25 to 34 comprising the following steps:

a. optionally expressing an FrpB protein in a host cell;

optionally breaking the host cell to obtain an inclusion body comprising the FrpB protein; optionally washing the inclusion body;

b. optionally solubilisation of at least part of the inclusion body and the FrpB protein (preferably with Guanidinium hydrochloride);

c. contacting the solubilised FrpB protein with the refolding buffer; and

d. optionally removing (or changing) the refolding buffer from the FrpB protein.

36. A refolding buffer comprising ethanolamine, SB-12 and, optionally, guandinium chloride for use in the method of any one of claims 25 to 35.

37. An isolated, refolded FrpB protein obtained or obtainable by the method of any one of claims 25 to 35.

38. A pharmaceutical composition comprising at least one FrpB protein of any one of claims 1 to 20 and 37, and a pharmaceutically acceptable carrier.

39. A pharmaceutical composition according to claim 38 wherein at least 30%, 50%, 70%, or 90% of the FrpB protein present in the composition is refolded.

40. A pharmaceutical composition according to claim 38 or 39 in the form of a vaccine.

41. The pharmaceutical composition of any one of claims 38 to 40 comprising a FrpB protein derived from *Neisseria meningitidis*.

42. The pharmaceutical composition of any one of claims 38 to 41 comprising a FrpB protein derived from *Neisseria gonorrhoeae*.

43. The pharmaceutical composition according to any one of claims 38 to 42 wherein said composition comprises at least one other Neisserial antigen.

44. The pharmaceutical composition of claim 43 comprising at least one other Neisserial antigen derived from *Neisseria gonorrhoeae*.

45. The pharmaceutical composition of claim 43 or 44 comprising at least one other Neisserial antigen derived from *Neisseria meningitidis*.

46. The pharmaceutical composition of any one of claims 38 to 45 in the form of a subunit composition.

47. The pharmaceutical composition of any one of claims 38 to 45 in the form of an outer membrane vesicle preparation, or a mixed subunit plus outer membrane vesicle preparation.

48. A pharmaceutical composition according to any one of claims 38 to 47 further comprising at least one other Neisserial antigen selected from one or more of the following classes:

a. at least one Neisserial adhesin selected from the group consisting of FhaB, NspA, Hsf, NadA, PilC, Hap, MafA, MafB, Omp26, NMB0315, NMB0995 and NMB1119;

b. at least one Neisserial autotransporter selected from the group consisting of Hsf, Hap, IgA protease, AspA and NadA;

c. at least one Neisserial toxin selected from the group consisting of FrpA, FrpC, FrpA/C, VapD, NM-ADPRT, and either or both of LPS immunotype L2 and LPS immunotype L3;

d. at least one Neisserial Fe acquisition protein selected from the group consisting of TbpA high, TbpA low, TbpB high, TbpB low, LbpA, LbpB, P2086, HpuA, HpuB, Lipo28, Sibp, FbpA, BfrA, BfrB, Bcp, NMB0964 and NMB0293; and

e. at least one Neisserial membrane associated protein, preferably outer membrane protein, selected from the group consisting of PldA, NspA, TspA, FhaC, NspA, TbpA(high), TbpA(low), LbpA, HpuB, TdfH, PorB, HimD, HisD, GNA1870, OstA, HlpA, MltA, NMB 1124, NMB 1162, NMB 1220, NMB 1313, NMB 1953, HtrA, TspB, PilQ and OMP85.

49. The pharmaceutical composition of any one of claims 38 to 48 further comprising one or more bacterial capsular polysaccharides or oligosaccharides.

50. The pharmaceutical composition of claim 49 wherein the one or more capsular polysaccharides or oligosaccharides is derived from bacteria selected from the group consisting of *Neisseria meningitidis* serogroup A, C, Y, and/or W-135, *Haemophilus influenzae* b, *Streptococcus pneumoniae*, Group A Streptococci, Group B Streptococci, *Staphylococcus aureus* and *Staphylococcus epidermidis*, and are preferably conjugated to a source ot T-helper epitopes.

51. Use of an FrpB protein of any one of claims 1 to 20 and 37 (or a pharmaceutical composition of claims 38 to 50) in the preparation of a medicament for use in generating an immune response in an animal.

52. Use of an FrpB protein of any one of claims 1 to 20 and 37 (or a pharmaceutical composition of claims 38 to 50) in the preparation of a medicament for treatment or prevention of Neisserial infection.

53. A method of preventing or treating Neisserial infection by administering an FrpB protein of any one of claims 1 to 20 and 37 (or a pharmaceutical composition of claims 38 to 50) to a patient in need thereof.

54. The use or method of claim 52 or 53 in which *Neisseria meningitidis* infection is prevented or treated.

55. The use or method of claims 52-54 in which *Neisseria gonorrhoeae* infection is prevented or treated.

56. An antibody immunospecific for the FrpB protein as claimed in any one of claims 1 to 20 and 37.

57. A pharmaceutical composition useful in treating humans with a Neisserial disease comprising at least one antibody according to claim 56 and a suitable pharmaceutical carrier.

58. Use of the antibody of claim 56 (or a composition of claim 57) in the manufacture of a medicament for the treatment or prevention of Neisserial disease.

59. The use of claim 58 in which *Neisseria meningitidis* infection is prevented or treated.

60. The use of claim 58 or 59 in which *Neisseria gonorrhoeae* infection is prevented or treated.

61. A method of diagnosing a Neisserial infection, comprising the steps of identifying an FrpB protein, or an antibody thereto, within a biological sample from an animal suspected of having such an infection using a FrpB protein as claimed in any one of claims 1 to 20 and 37, or an antobody as claimed in claim 56.

62. The method of claim 61 in which *Neisseria meningitidis* infection is diagnosed.

63. The method of claim 61 or 62 in which *Neisseria gonorrhoeae* infection is diagnosed.